REMARKS

Claims 13 and 29 have been amended in response to the formal rejections. The wording of claim 13 has been changed, as kindly recommended by the Examiner, and claims 13 and 29 have been amended to specify that the nucleic acid and assistor protein or a nucleic acid and influenza HA protein are "associated with the same liposomes" rather than "co-encapsulated." This is not new matter since it is language similar to that used in the specification on page 4, lines 25-27, and page 7, lines 31-36, for example. This obviates the rejection of these claims under 35 U.S.C. § 112, paragraph 2.

Claims 13 and 29 have also been amended to require that the "liposomes are not polymerized and are based substantially on phospholipids." Support for the liposomes being based substantially on phospholipids is found on page 7, at lines 25-27. There is no *in haec verba* support for the requirement that the liposomes are "not polymerized." However, this disclosure is inherent in the specification and not new matter. All of the liposomal compositions described generically and exemplified lack a polymerization step.

It is well-recognized that a feature that is inherent in the disclosure need not be explicitly disclosed in order to be claimed explicitly. For example, in *Kennecott Corp. v. Kyocera Int'l, Inc.*, 835 F2d 1419, 5 USPQ2d 1194 (Fed. Cir. 1987), claims were directed to a sintered ceramic body that explicitly required "equiaxed" microstructures. There was no explicit disclosure of equiaxed microstructures in the parent application from which priority was claimed. Nevertheless, priority was granted because the preparation of the same materials was described and they inherently have this property.

Thus, the Court decided that the priority document supported the claim term because the property now made explicit was inherently present. This is precisely the case here.

New claims 32 and 33 are supported on page 19 of the specification at lines 31-34.

New claims 34 and 35 are supported on page 19 of the specification at lines 9-12.

Entry of the amendment is respectfully requested.

The Rejection Over the Art

There is one rejection over the art and it is applied to all claims, claims 13, 16 and 25-31, over the combination of Craig, *et al.* (WO97/28818) in view of Gregoriadis, *et al.* ((1999) *Methods* 19:156-162); Nagy, *et al.* (U.S. 7,285,289); and Gregoriadis, *et al.* (2006) (U.S. 7,008,791).

Applicants note with appreciation that the previous amendments to the claims, which require that the antigenic protein is displayed on the surface of the liposomes, that the nucleic acid is entrapped in the intravesicular space, and that a cationic lipid render the liposomes positively charged have necessitated the addition to the documents previously made the basis for rejection, the disclosures of Nagy, *et al.*, and of Gregoriadis (2006). Nagy is evidently cited under 35 U.S.C. § 102(e) based on the filing date of provisional application 60/372,631 filed April 12, 2002, just ahead of the date to which applicants are entitled of July 5, 2002. Like Nagy, Gregoriadis (2006) is cited under § 102(e) based on a date just slightly before the date to which provisional applicants are entitled.

Nagy and Gregoriadis (2006) are cited assertedly to remedy the deficiencies in the originally cited documents, which fail to require that nucleic acid and protein be associated with the same liposomes in such a way that the nucleic acid is in the interior and the antigenic protein is displayed

on the surface and that a cationic lipid be included. If these documents do not properly remedy this deficiency, the rejection must fall on this basis alone.

Nevertheless, the Office appears to read more into the disclosure of Craig and Gregoriadis (1999) than actually is disclosed. The Office refers to page 12 of Craig as disclosing the use of liposomes for the delivery of DNA and protein to cells. Craig does not say this. When discussing the delivery of "protein associated with nucleic acid" delivery to a mammalian cell, Craig describes DNA/polycation complexes, self-assembling virus-like particles, and viral vectors. When discussing the delivery of DNA *or* protein to cells, only then are liposomes referred to. Craig clearly does not specifically suggest the use of liposomes to deliver nucleic acids as associated with peptides to cells using liposomes. Craig is the only cited document that even discusses using a combination of nucleic acid and antigenic peptide. Craig fails to make any suggestion that these be associated with the same liposome and thus falls short. The remaining documents do not remedy this because they, too, fail to suggest associating both nucleic acids and proteins with liposomes.

Nagy is cited only for describing surface display of protein. If Nagy fails to teach surface display of a protein on liposomes as claimed in the present case, Nagy fails to disclose this essential feature of the invention, and as no other document is cited for this proposition, the entire basis for rejection fails. That is, in order for the rejection to be sustained, Nagy must teach the surface display of a protein on liposomal compositions.

Respectfully, Nagy does not teach this. Nagy is directed specifically to polymerized liposomes and discusses at length the disadvantages of phospholipid-based liposomes that are not polymerized. An extensive list of such disadvantages appears beginning in column 2, at line 46, and

continuing to column 3, line 46. Nagy specifically teaches away from displaying a peptide at the surface of a liposome, as claimed in the present case.

Claims 13 and 29 explicitly exclude the nanoparticles described by Nagy, as they are required to be unpolymerized and to be based substantially on phospholipids. Nagy explicitly teaches away from displaying a protein on the surface of an unpolymerized liposome based substantially on phospholipids.

Nagy also teaches away from the invention in another sense, in that any nucleic acid contained in the particles of Nagy is also required to be at the surface, rather than the intravesicular space. See column 11 at lines 50-54. Thus, not only does Nagy teach away from the surface displayed protein on phospholipid-based unpolymerized liposomes, Nagy also teaches away from the claim requirement that nucleic acid be included in the intravesicular space. While the Office cites another document for this (Gregoriadis 2006), this cannot be reconciled with the negative teaching of Nagy – that nucleic acids should be displayed at the surface of a particle.

Since Nagy is the only document cited to teach display of protein at the surface of liposomes and it fails to do so, rather teaching that the protein should only be displayed at the surface of polymerized liposomes, the rejection should be withdrawn based on this failure of Nagy alone.

Where liposomes that are not polymerized are used as a basis, display at the surface is actually taught away from. Gregoriadis (1999) is directed to the entrapment of peptides in liposomes, as opposed to display on their surface.

The requirement that the liposomes include at least one cationically charged component such that the liposomes have an overall positive charge and have nucleic acid in their intravesicular space, has apparently required the addition of Gregoriadis (2006).

The focus of Gregoriadis (2006) is oral nucleic acid vaccines.* The nucleic acid, while permitted, and even preferred, to be entrapped is not required to be in the intravesicular space. The nucleic acid may merely be complexed with the cationic lipids. Because Gregoriadis (2006) is directed to an oral vaccine specifically, the practitioner reading Gregoriadis (2006) would not be motivated to provide anything other than an oral vaccine. Claims 32 and 33 exclude oral vaccines, so they are clearly free of this art and therefore this rejection.

In addition, Gregoriadis (2006) teaches away from any combination with Nagy (which combination is required in order to support the present rejection) by stating in column 5, at lines 28-31, that the invention does not involve polymerizing the liposome-forming components, which is the whole point of Nagy.

In summary, the two newly added documents fail to remedy the deficiencies in the two documents originally cited. Gregoriadis (2006) specifically teaches away from combining its teachings with those of Nagy. Nagy fails to teach the incorporation of nucleic acids into the intravesicular space as well as specifically discouraging the use of unpolymerized liposomes encompassed by the claims, and required by Gregoriadis (2006).

Since these documents fail to remedy the acknowledged deficiencies of the originally cited documents, the rejection should be withdrawn.

* This document mentions WO98/10748, of record herein, which describes liposomal nucleic acid vaccines in cationic liposomes for parenteral administration.

Conclusion

In view of the failure of the newly cited documents to remedy the deficiencies in the documents originally cited, applicants believe the rejection should be withdrawn and claims 13, 16, 25-26, 28-30 and 32-35 be passed to issue.

Should minor issues remain that could be resolved by phone, a telephone call to the undersigned is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 429022000800.

Respectfully submitted,

Dated: December 30, 2008 By: / Kate H. Murashige /

Kate H. Murashige
Registration No.: 29,959
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
Telephone: (858) 720-5112
Facsimile: (858) 720-5125